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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/024,933	12/18/2001 .	Olga Bandman	PF-0352-2 DIV	4096

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EXAMINER
HUTSON, RICHARD G

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 04/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/024,933	BANDMAN ET AL.	
	Examiner	Art Unit	
	Richard G Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *1-13 and 17-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/6/2004 has been entered.

Applicants request to enter the previously un-entered amendment filed on 12/23/2003 and the accompanying declaration of Dr. Tod Bedilion under 37 C.F.R. 1.132 are acknowledged. Applicants previous amendment of 12/23/2003 has been entered. Additionally on page 2 of applicants response accompanying the request for continued examination, under a remarks heading, applicants state:

> "In further response to the Final Office Action dated November 4, 2003, Applicants filed a Submission accompanying a Request for Continued Examination (RCE) of U.S. Application Number 10/024,933 on February 4, 2004. Therefore, this communication is moot in view of the RCE, and the amendments previously submitted should now be considered in the RCE."

This statement is confusing to the examiner, who called applicant's representative for clarification on 4/15/2004. Mr. James Verna agreed that this statement is confusing and stated that applicants intent was to have the previous submitted arguments of 12/23/2003 considered. It is further noted to applicant that the declaration submitted on 12/23/2003 is a signed copy of the unsigned declaration submitted on 8/21/2003 with the exception that the declaration submitted on 12/23/2003

is missing the first three lines from the declaration submitted on 8/23/2003 (i.e. from "I understand that " to "technology that was being").

Claims 1-20 remain at issue and are present for examination. Applicants amendment of claims 14 and 16, Paper of 12/23/2003, is acknowledged.

Applicants' arguments filed on 12/23/2003, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claims 1-13 and 17-20 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 6.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14-16 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection was stated in the previous office action as it applied to previous claims 14-16. In response to this rejection applicants have amended claims 14 and 16 and traverse the rejection as it applies to the newly amended claims. Applicants amendment of claims 14 and 16 part b) to recite "said polynucleotide encodes a polypeptide having methyltransferase activity" and the deletion of the phrase "and which probe specifically hybridizes to said target polynucleotides" in claim 14 is acknowledged.

Applicants traverse the rejection on the following basis. Applicants submit that the specification provides an adequate written description of the structure of the target polynucleotides of the claims, through the recitation of chemical structure and that no description of the function of the polynucleotides is required to satisfy the written description requirement for the claimed methods of detecting the target polynucleotides because disclosure of functional characteristics is merely one of the factors which can be used as evidence that Applicants were in possession of the claimed invention at the time of filing. Applicants submit that such functional limitations are not necessary as structural and source limitations are sufficient to describe the target polynucleotides and further "biological function" is irrelevant to the use of the claimed methods. This argument is not found persuasive because while it is acknowledged that functional limitations are but one of the factors used as evidence that applicants were in possession of the claimed invention, applicants have provided no additional evidence or rather limitations of the claimed invention other then the structure of SEQ ID NO: 2. As previously said, the specification only provides the representative methods

encompassed by the claims in which the target polynucleotide and comprises SEQ ID NO: 2. Applicants have not limited the claimed methods to include the above submitted structural and source limitations which applicants state are sufficient to describe the target polynucleotides without any evidence of such. The mere description of structural attributes of the target polynucleotides (i.e. sequence identity to SEQ ID NO: 1) is insufficient to sufficiently describe the claimed methods. While limitation to a functional characteristic for a claimed polynucleotide or method of detecting such may not be necessary, applicants have not met sufficiently the additional means of describing the claimed methods of detecting said target polynucleotides.

Applicants are further reminded that while applicants have described methods encompassed by the claims comprising the use of SEQ ID NO: 2 and fragments of SEQ ID NO: 2, applicants have not described the genus of methods which are drawn to those methods of use of probes comprising at least 20 contiguous nucleotides comprising a sequence complementary to said target polynucleotide, wherein said target polynucleotide comprises a naturally occurring polynucleotide sequence at least 90% identical to SEQ ID NO: 2 and encodes a polypeptide having methyltransferase activity.

Applicants comments regarding the original rejection of the claims which were directed to **all** possible methods for detecting **any** target polynucleotide of previous claim 12 are acknowledged, as is applicants **newly** submitted amendment of these claims.

Applicants comments regarding that one of ordinary skill in the art would recognize polynucleotide sequences which are variants at least 90% identical to SEQ ID

NO: 2 and that given any naturally occurring polynucleotide sequence, it would be routine for one of skill in the art to recognize whether it was a variant of SEQ ID NO: 2 are acknowledged, however, not found persuasive. Applicants argue that "given a naturally occurring polypeptide sequence", one would be able to recognize whether it was a variant of SEQ ID NO: 2. Applicants have only "given one naturally occurring polynucleotide sequence", that comprising the nucleic acid sequence of SEQ ID NO: 2. Applicants argument is not found persuasive because the question is not whether one would be able to determine whether a given naturally occurring polypeptide is a variant of SEQ ID NO: 1, but rather have appellants described said naturally occurring polynucleotides sufficiently and methods of their detection, that one of skill in the art would recognize that Applicant was in possession of said methods of detecting naturally occurring polypeptide variants of SEQ ID NO: 1. As stated previously and above appellants have merely described a single naturally occurring polynucleotide (i.e. that polynucleotide comprising the nucleic acid sequence of SEQ ID NO: 2).

Applicants argue that the present claims specifically define the claimed genus through the recitation of chemical structure and the present claims do not define a genus which is "highly variant" and present the reference Brenner et al. (PNAS Vol 95: 6073-6078, 1998) in support of this position. Applicants submit that Brenner et al. have determined that 30% identity is a reliable threshold for establishing evolutionary homology between two sequences aligned over at least 150 residues. Applicants argue that therefore "naturally occurring molecules" may exist which could be characterized as SAM-MT proteins and which have as little as 40% identity over a region of at least 70

residues of SEQ ID NO: 1. While it may be that an evolutionary relationship may exist between two molecules with as little as 40% identity over a region of at least 70 residues, this does not in any way reflect on the description of those naturally occurring molecules or whether a single species is representative of the claimed naturally occurring molecules or methods of their detection.

Applicants further argue that the state of the art at the time of the present invention is further advanced than at the time of the *Lilly* and *Fiers* applications and the written description decisions based on these cases. Applicants submit that based on the developments in the field of recombinant DNA technology since these decisions (i.e. the "dark ages" of recombinant DNA technology), one of skill in the art would recognize that given the sequence information of SEQ ID NO: 1 and the additional extensive detail provided by the subject application, the present inventors were in possession of the target polynucleotides of the claims. These arguments are not found persuasive. Applicants argument appears to be directed towards whether one of skill in the art would be able to "obtain" a "naturally occurring nucleic acid sequence". Applicants argument does not help in their rebuttal that given the lack of representative species as encompassed by the claims, applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize applicants were in possession of the claimed invention.

Therefore, the instant claims are not adequately described.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 14-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed hybridization and amplification methods of detection of a target polynucleotide, using a polynucleotide consisting of SEQ ID NO: 2 and fragments thereof as a hybridization probe or an amplification primer, wherein the target polynucleotide comprises SEQ ID NO: 2 which encodes a methyltransferase, does not reasonably provide enablement for any hybridization or amplification method of detection of a target polynucleotide, using any polynucleotide comprising at least 20 contiguous nucleotides complementary to said target polynucleotide as a hybridization probe or any amplification primer, wherein the target polynucleotide comprises a naturally occurring sequence at least 90% identical to SEQ ID NO: 2, wherein said target encodes a methyltransferase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

This rejection was stated in the previous office action as it applied to previous claims 14-16. In response to this rejection applicants have amended claims 14 and 16 and traverse the rejection as it applies to the newly amended claims. Applicants amendment of claims 14 and 16 part b) to recite "said polynucleotide encodes a polypeptide having methyltransferase activity" and the deletion of the phrase "and which

probe specifically hybridizes to said target polynucleotides" in claim 14 is acknowledged. Applicants continue to traverse the rejection for the reasons made of record in the response filed on 8/21/2003.

Applicants comments on page 15, in the second paragraph of applicants current response to the enablement rejection, in which applicants state:

> "In addition, since the current amendments limit the claimed invention to methods of detecting the polynucleotide sequence of SEQ ID NO: 2, Applicants believe that the Examiner should find the Specification enabling in light of the current amendments."

are confusing since the current amendments limit the methods of detection to those polynucleotides 90% identical to SEQ ID NO: 2, not SEQ ID NO: 2.

Applicants submit that the disclosure amply enables the claimed invention. Given the sequence of SEQ ID NO: 2, one of ordinary skill could readily identify a polynucleotide encoding a polypeptide comprising a naturally occurring polynucleotide comprising a naturally occurring polynucleotide sequence at least 90% identical to a polynucleotide sequence of SEQ ID NO: 2

With respect to "How to make" applicants disclose SEQ ID NO: 1 and SEQ ID NO: 2 and submit that given this, the specification describes how to find those "Naturally occurring" polynucleotides to be used by the claimed methods. While applicants argument of "How to make" is found sufficient for those methods of detection using probes consisting of SEQ ID NO: 2 and fragments of SEQ ID NO: 2 applicants have not enabled those methods of use of probes comprising a sequence complementary to said target polynucleotide, wherein said target polynucleotide comprises any naturally occurring polynucleotide sequence at least 90% identical to a polynucleotide sequence

of SEQ ID NO: 2 wherein said target polynucleotide encodes a polypeptide having methyltransferase activity. Applicants have not enabled the broad genus of probes necessary to practice the claimed methods.

With respect to "How to use", applicants submit that the invention is directed, *inter alia*, to methods of detecting polynucleotides encoding polypeptides having homology to *Caernorhabditis elegans* putative methyltransferase (GI 1065505) and that the claimed methods and target polynucleotides have a variety of utilities, in particular in expression profiling and in particular for diagnosis of conditions or diseases characterized by expression of SEQ ID NO: 1 (SAM-MT), for toxicology testing and for drug discovery.

Applicants submit that the invention at issue includes methods for detecting polynucleotide sequences corresponding to a gene that is expressed in a PMA + LPS stimulated THP-1 promonocyte cell line and as such the claimed invention has numerous practical, beneficial uses in toxicology testing, drug development, and the diagnosis of disease, none of which requires knowledge of how the polypeptide coded for by the polynucleotide detected by the claimed methods actually functions. In support of applicants assertions applicants submit the unexecuted declaration of Tod Bedilion describing the practical uses of the claimed invention in gene and protein expression monitoring applications.

Applicants assert as such the claimed invention has numerous practical, beneficial uses in toxicology testing, drug development, and the diagnosis of disease,

none of which requires knowledge of how the polypeptides [en]coded for by the polynucleotides actually function.

Applicants further assert that the law never has required knowledge of biological function to prove utility, and that it is the claimed invention's uses, not its functions, that are the subject of a proper analysis under the enablement requirement. Applicants submit that the uses of the claimed methods for diagnosis of conditions and disorders characterized by expression of SAM-MT for toxicology testing and for drug discovery and that these are sufficient utilities under 112 first paragraph. Applicants submit within the declaration by Tod Bedilion, a number of references that discuss the benefits of these various methodologies such as "differential gene expression","toxicogenomics" and "expression profiling", but applicants give no guidance as to how those claimed polynucleotides which do not encode a polypeptide having SAM-MT activity are so useful. Applicants disclose no specific examples of such uses, but rather assert that the claimed methods of detecting polynucleotides, a majority of which have no "functional" limitation, may be useful for such general techniques as "expression profiling" and "drug development". Applicants give none of the particulars of toxicology testing with the claimed methods of detecting naturally occurring polynucleotides having greater than 90% identity to SEQ ID NO: 2. Neither the toxic substances nor the susceptible organ systems are identified. Therefore, this is a utility which would apply to virtually every member of a general class of materials, such as any collection of proteins or polynucleotides, but is only potential with respect to the claimed polynucleotides. Further any potential diagnostic utility is not yet known and has not yet been disclosed.

Applicants argue that in recent years, techniques have been developed for toxicology testing, drug development, and disease diagnosis. Applicants argue these techniques rely on gene expression profiling by analyzing the relative levels of genes or proteins present in two or more samples. Applicants argument has been considered but is not found persuasive to overcome the rejection.

While it is well-established that techniques such as toxicology testing, drug development, and disease diagnosis may be useful, as previously stated, the instant specification has not established the claimed polynucleotide variants (or even SEQ ID NO:1/@) as having altered expression levels or expressed in altered forms in a diseased cell or tissue relative to the corresponding healthy cell or tissue. The instant specification has not established increased expression levels or forms of any of the disclosed polynucleotides and therefore, undue experimentation would be required to use the claimed polynucleotide variants for the asserted uses. Therefore, methods of detecting polynucleotide variants as encompassed by the claims will not necessarily be useful in the same fashion as SEQ ID NO:1/2 nor in toxicology testing, drug development, and disease diagnosis as argued by appellants and, in fact, the vast majority of such variants may not be useful at all. As such, the scope of the claims remains broader than the scope of the enabling disclosure.

Appellants' arguments have been fully considered but are not found persuasive to overcome the rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 14-16 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Bokar et al. (Journal of Biological chemistry, Vol. 269, No. 26, pages 17697-17704, 1994, See IDS, Ref No. 5) and Hillier et al. (Wash-Merck EST Project, GENBANK Accession Number AA054310, December 1996).

The rejection was stated in the previous office action of 5/16/2003 and maintained in the office action of 11/4/2003 and repeated below for applicants convenience.

Bokar et al. teach that the widespread presence of m^6A in mRNA from diverse higher eukaryotic species, along with the striking RNA sequence requirements for methylation, suggests that m^6A and the enzyme responsible for its occurrence in RNA may play an important role in mRNA metabolism. Bokar et al. teach the characterization and partial purification of mRNA N^6-adenosine methyltransferase from Hela Cell Nuclei. Bokar et al. further teach that the characterization and cloning of the genes that encode the individual subunits of this multicomponent enzyme will allow a better understanding of the underlying complexity of this enzymatic activity and the biological function of the post-transcriptional modification it produces.

Hillier et al. (Wash-Merck EST Project, GENBANK Accession Number AA054310, December 1996) disclose a 463 nucleotide human cDNA fragment which

encodes a methyltransferase and has a best local similarity score of 98.2% to the complement of SEQ ID NO: 2, between nucleotide 682 and nucleotide 1128.

One of ordinary skill in the art would have been motivated to use the nucleotide sequence information disclosed by Hillier et al. to detect and isolate a full length human methyltransferase cDNA clone, to lead to a better understanding of the underlying complexity of the methylation of nucleic acids as a post-transcriptional modification mechanism. This motivation comes from the art as well as the teachings of Bokar et al. who state "characterization and cloning of the genes that encode the individual subunits of this multicomponent enzyme will allow a better understanding of the underlying complexity of this enzymatic activity and the biological function of the post-transcriptional modification it produces". Further the cloning of the gene(s) encoding will further the understanding of the process of the methylation of nucleic acids by allowing the enzyme responsible for this process to be produced recombinantly. The many advantages of recombinant production of useful proteins are well known within the art as are recombinant methods of obtaining the necessary genes. These advantages include the ability to produce much larger quantities of the protein, being able to produce the protein in more easily handled organisms, reducing the number of steps necessary for the purification of a protein and producing the protein in a purer form by using an organism that does not include naturally occurring contaminants of the protein.

One of ordinary skill in the art would have been motivated to use any of a number of commonly used techniques to detect and isolate the full length gene(s) such as methods based on hybridization or methods based on polymerase chain reaction

amplification. Those methods based on hybridization would involve the use of the cDNA fragment taught by Hillier et al. as a nucleic acid probe, hybridizing a sample with the probe under conditions whereby a hybridization complex is formed between said probe and a target polynucleotide and detecting the presence of said hybridization complex. Those methods based on polymerase chain reaction amplification would involve the use of the cDNA fragment taught by Hillier et al. to design nucleic acid primers for use in a polymerase chain reaction, amplifying a target polynucleotide in a sample using the designed primers and detecting the presence of said amplified target polynucleotide. The reasonable expectation of success comes from the high degree of knowledge in the art with respect to the identification and detection of polynucleotides using both hybridization and polymerase amplification methodologies and the teachings of Bokar et al. and Hillier et al. who teach that human cells have at least one methyltransferase and thus its encoding polynucleotide. Based on the high degree of similarity between the clone taught by Hillier et al. and instantly disclosed SEQ ID NO: 2 (i.e. greater then 98%), each of the above methods of detection would detect a polynucleotide having the sequence of SEQ ID NO: 2 (encompassed by the polynucleotide of claim 12) and thus the claimed methods are made obvious by Bokar et al. and Hillier et al.

Applicants continue to traverse this rejection for the reasons made of record in applicants response filed on 8/21/2003 and for the reasons repeated below.

Applicants submit that SEQ ID NO: 2 is 672 nucleotides longer than to Hillier fragment and that the Hillier et al. reference does not disclose that the cited AA054310

fragment encodes a methyltransferase. Applicants are reminded that the entire sequence of SEQ ID NO: 2 is unnecessary to practice the invention of claims 14-16 and that Hillier et al. teach that the encoded polypeptide is a putative methyltransferase.

Applicants submit that the current amendments limit the claimed invention to methods of detecting the polynucleotide sequence of SEQ ID NO: 2 and this sequence is not disclosed by the cited reference(s) and the Hillier et al. reference does not teach or suggest the entirety of applicants claimed invention, therefore there would be no motivation to combine the cited references and claims 14-16 cannot be rendered obvious. Applicants submit that the Hillier et al. reference does not disclose that the cited AA054310 fragment encodes a methyltransferase and the Bokar et al. reference does not disclose any sequence. Applicants arguments are not found persuasive, because while the Hillier et al. reference does not disclose that the cited AA054310 fragment encodes a methyltransferase, they do putatively identify the encoded protein as a methyltransferase. While Boklar et al. do not teach any sequence, they do teach that the enzyme responsible for methylation may play an important role in mRNA metabolism and that the characterization and cloning of the genes that encode the individual subunits of this multicomponent enzyme will allow a better understanding of the underlying complexity of this enzymatic activity and the biological function of the post-transcriptional modification it produces. It is the associated teachings of each of the references as they relate to methyltransferases that provide the motivation to combine and what one reference suggests (Bokar et al.) the other reference (Hillier et al.) provides the tools for accomplishing.

Applicants further submit that each of the rejected claims as currently amended are drawn to methods of detecting specific polynucleotides wherein said polynucleotide has the sequence of a polynucleotide of previous claim 12, now which have been incorporated into claims 14-16. Applicants submit that this limitation, presumably applicants are referring to the sequence of the target polynucleotide, is not taught by the prior art.

Applicants submit that the examiner has mischaracterized the claims and that in all three rejected claims, drawn to methods of detecting, the preamble contains the implicit limitation "said target polynucleotide having a sequence of a polynucleotide of claim 12.

Applicants argument is not found persuasive for the following: In response to applicants assertion that the examiner has mischaracterized the claims, while it is acknowledged that the combination of the above references may not make obvious a specific particular sequence, the rejected claims are not directed to a specific particular sequence but rather a method of detecting a genus of polynucleotides. As previously stated the combination of Bokar et al. and Hillier et al. would make obvious a method which would comprise each of the steps of the claimed methods. This made obvious method would encompass a method of detecting those polynucleotides at least 90% identical to a polynucleotide sequence of SEQ ID NO: 2, thus the inclusion of the preamble of claims 14 and 16 as a part of the claimed methods does not make applicants claimed methods non-obvious. Applicants are reminded that the claims are

not directed to specific particular polynucleotides but rather to "methods of detecting polynucleotides", the sequence of which may be inherent.

In response to applicant's arguments, the recitation "for detecting a target polynucleotide in a sample, said target polynucleotide..." has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

Applicants further argue that the examiner has failed to establish a prima facie case of obviousness based on the following: Applicants assert that the nucleic acid sequence of SEQ ID NO: 2 was not known until applicants elucidated it. In response to this argument applicants are reminded that the sequence of SEQ ID NO: 2 is not necessary to practice the claimed methods as discussed previously and above.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a

reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Applicants further argue that the examiner alleges that the method of detecting a polynucleotide of SEQ ID NO: 2 is obvious because a human cDNA fragment encoding a methyltransferase was identified. Applicants argument is not persuasive because in the earlier rejection the examiner stated that it would have been obvious for one of ordinary skill in the art to use the nucleotide sequence information disclosed by Hillier et al. to detect and isolate a full length human methyltransferase cDNA clone, not the specific polynucleotide of SEQ ID NO: 2. SEQ ID NO: 2 is merely an inherent property of a full length human methyltransferase cDNA clone. As discussed above it is the method that is obvious, not the polynucleotide which is detected by said obvious method.

Remarks

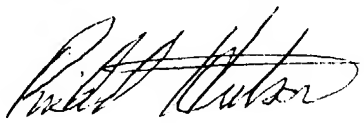
No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned

are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rgh
April 16, 2004